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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/142,043	12/01/98	MOSSAKOWSKA	D 88362/104

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EXAMINER	
HAMUD, F	
ART UNIT	**PAPER NUMBER**
1646	11

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

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1- File Copy

Art Unit

Application No.	Applicant(s)
09/142,043	MOSSAKOWSKA et al.
Examiner	**Group Art Unit**
Fozia Hamud	1646

Office Action Summary

☒ Responsive to communication(s) filed on *Jun 17, 1999*.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *37-57* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *37-57* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☒ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☒ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *6*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- ***SEE OFFICE ACTION ON THE FOLLOWING PAGES*** ---

DETAILED ACTION

1. Claims 1-36 have been canceled and new claims 37-65 have been added in Paper No.7 filed on 3/3/99. Claims 58-65 have been canceled in Paper No.8 filed on 03/31/99. Claims 37-57 are pending and under consideration by the Examiner.

Specification

2a. It is noted that this application appears to claim subject matter disclosed in prior PCT Application No. PCT/EP97/00994, filed on 12/24/96 (now WO 97/31944, issued 09/04/97). A reference to the prior application must be inserted as the first sentence of the specification of this application if Applicant intends to rely on the filing date of the prior application under 35 U.S.C. 120. See 37 CFR 1.78(a).

It is suggested that below the title of the invention be inserted:

Cross Reference to Related Applications

"This Application is a 371 of WO97/31944".

Appropriate correction is required.

2b. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

Claim objections

3. Claims 37, 43, 48, 51, 53, 54 and 57 are objected to because of the following informalities:

Claims 37, 43, 48, 51, 53, 54 and 57 recite both the actual amino acid sequences and the SEQ ID Nos for the claimed polypeptides. The recitation of the actual amino acid sequences and the SEQ ID Nos in the claims is redundant and renders the claims unclear. It is suggested that the recitation

of the actual amino acid sequences be deleted and the polypeptides be identified only with the appropriate SEQ ID Nos. With respect to the claims drawn to fragments of the claimed polypeptides, the recitation of, for example "residues 6-11 of SEQ ID NO:1" is sufficient.

Appropriate correction is required.

Claim rejections-Double patenting

Non-statutory double patenting rejection (obviousness-type)

4. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321© may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4a. Claims 37, 51 and 57 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 2 and 10 of U.S. Patent No. 5,833,989. Although the conflicting claims are not identical, they are not patentably distinct from each other. The claims in the instant application claim a SCR3-derived polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 1, 4, 5, 7 and 8, and a pharmaceutical composition comprising the SCR3-derived polypeptide with the amino acid sequence set forth in SEQ ID NO:1. Claims 2 and 10 of U.S. patent NO.5,833,989 (having two common inventors with the instant application), claim a soluble polypeptide comprising no more that one short consensus repeat (SCR) of long homologous repeat A of complement Receptor 1, wherein the polypeptide comprises SCR3 and a pharmaceutical composition comprising said polypeptide. The instant claims 37, 51 and 57, are species to claims 2 and 10 in the patent which encompass the subject matter of the instant claims. The instant claims are obvious from the patent claims because the patent is directed to genus subject matter in which the instant claims are one specific embodiment. The instant claims are included in the patented product. It would have been obvious to one of ordinary skill in the art at the time the present invention was made, that a soluble polypeptide comprising no more than one short consensus repeat (SCR) of long homologous repeat A of complement Receptor 1, wherein the polypeptide comprises SCR3, includes an SCR3-derived polypeptide, because the term "comprising" in the patented claims denotes open language, encompassing the instant species claims. The instant claims if infringed upon would also result in infringement of the broad claims of the patent. Allowance of the pending claims, therefore, would have the effect of extending the enforceable life of the allowed claims beyond statutory limit.

Claim Rejections - 35 U.S.C. § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5a. Claims 37-57, are rejected under 35 U.S.C. 112, first paragraph, because the specification while being enabling for an isolated polypeptide consisting of amino acid residue 154 to amino acid residue 186 of the third short consensus repeat (SCR3) region of the human complement receptor type 1 (CR1), wherein said polypeptide is selected from the group consisting of: an isolated polypeptide with the amino acid sequence set forth in SEQ ID NO:1, wherein said polypeptide consists of at least amino acid residues 6-11 or amino acid residues 11-20 of SEQ ID NO:1, said polypeptide further comprising a cysteine residue at the carboxyl and the amino terminuses, wherein the carboxyl terminus cysteine is derivatized with S-(2-pyridyl) dithio, a linear polypeptide with the amino acid sequence set forth in SEQ ID NO:4, a cyclic polypeptide with the amino acid sequence set forth in SEQ ID NO:4, an isolated polypeptide with the amino acid sequence set forth in SEQ ID NO:5, 7 and 8, said polypeptide having anti-complement activity; a multimeric polypeptide comprising two to eight polypeptides of the polypeptide with the amino acid sequence set forth in SEQ ID NO:1 linked to a core structure of lysine $(lys)_4$ $(lys)_2$ lys ala (set forth in SEQ ID NO:2) or tris (aminoethyl) amine and 1, 2, 4, 5 benzene tetracacrboxylic acid, or linked to a core structure of $(lys)_4$ $(lys)_2$ ala-OH (SEQ ID NO:6) through N-3-(2-pyrdyl)dithiopropionic acid-N-oxysuccinimide ester to cysteine thiol of the polypeptide with the amino acid sequence set forth in SEQ ID NO:5;

a chimeric polypeptide comprising a plasma protein and the isolated polypepitde with the amino acid sequence set forth in SEQ ID NO:1;a pharmaceutical composition comprising a therapeutically effective amount of an isolated polypeptide with the amino acid sequence set forth in SEQ ID NO:1 and a pharmaceutically acceptable carrier or excipient, and a process for preparing an isolated polypeptide with the amino acid sequence set forth in SEQ ID NO:1, following conventional solid peptide synthesis by condensing appropriate peptide units and thereafter chemically linking the polypeptide to a core structure, the specification is not enabling for "all" SCR3-derived polypeptides, or for a multimeric polypeptides comprising SCR3-derived polypeptides, or for "all" chimeric polypeptides comprising a host protein and SCR3-derived polypeptides, or a polynucleotide encoding the polypeptide with the amino acid sequence set forth in SEQ ID NO:1, or a process for preparing said polypeptide by expressing a polynucleotide encoding said polypeptide in a recombinant host cell and recovering the polypeptide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Claims 37, 43 and 48 recite "an SRC3-derived polypeptide having 6 to 23 amino acids....., a multimeric polypeptide comprising at least two SCR3-derived polypeptides.... and a chimeric polypeptide comprising a host protein and an SCR3-derived polypeptide.... " however, what is claimed in the instant invention broadly encompasses "all" polypeptides derived from the SCR3 region of the human CR1, or multimeric polypeptides comprising two or more polypeptides derived from the SCR3 region of the human CR1, or for "all" chimeric polypeptides comprising a host protein and a polypeptides derived from the SCR3 region of the human CR1. However, the specification

discloses that the polypeptides of the instant invention consist of amino acid 154 to amino acid 186 of the SRC3 region of the human CR1 (i.e between cysteine 154 and glycine 186), and that this polypeptide displays anti-complement activity. The specification also discloses that the polypeptide of the instant invention may be modified to have cysteine residues at the C and the N termini to provide (a) a cyclic molecule bridged by a disulfate bond, (b) a route for chemical linkage to other peptides to form mutimeric polypeptide for enhancing activity, (see page 4, lines 3-37, and page 22, line 4 through page 23, line 27) and this is the property which the protein is expected to exhibit, the specification is non-enabling for the unlimited number of polypeptides having this property, and which are encompassed by the scope of the claims. The specification also discloses a process for producing the polypeptide of the instant invention by condensing appropriate peptide units and thereafter optionally chemically linking the polypeptide with a core structure, (see page 9, lines 27-37, and pages 15-21). Since no material limitations for "all" the polypeptides have been recited in the claims, the claims encompasses every conceivable structure for achieving the stated property, a fact situation comparable to Hyatt. The claimed invention encompasses polypeptides not envisioned or described in the specification, and neither does the specification disclose how these claimed polypeptides can be distinguished from each other. The specification only enables polypeptide having the amino acid sequences shown in SEQ ID NO:1, SEQ ID NO:4 (linear and cyclic), SEQ ID NO:5, SEQ ID NO:7, and SEQ ID NO:8, the polypeptides having specific characteristics and properties. These properties may differ structurally, chemically and physically from other known proteins. By application of the factors set forth in Ex parte Forman (230 USPQ 546 (Bd. Pat. App. & Int. 1986), and reiterated in In re Wands (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)), which include (1) quantity

of experimentation, (2) guidance presented, (3) the predictability of the art, and (4) the breadth of the claims, in the instant application, the quantity of experimentation to determine which polypeptides comprising at least a portion or 6 to 23 amino acids of the amino acid sequence set forth in SEQ ID NO:1 are encompassed by the scope of the claims is practically infinite and the guidance provided in the specification very little. Therefore, it would require undue experimentation to determine which portion of the amino acid sequence set forth in SEQ ID NO:1 or multmeric polypeptide or chimeric polypeptide, having the desired biological activity, would be encompassed by the scope of the claims. The disclosure of the isolated polypeptide consisting of amino acid residue 154 to amino acid residue 186 of the third short consensus repeat (SCR3) region of the human complement receptor type 1 (CR1), is clearly insufficient support under the first paragraph of 35 U.S.C. § 112 for claims which encompass every and all polypeptides, including multimeric, chimeric and mutants thereof.

Furthermore, the amount of embodiments corresponding to the desirable polypeptides, may be innumerable, and the enabled embodiments amount to only those with amino acid sequences set forth in SEQ ID Nos: 1, 4, 5, 7 and 8. Therefore, there are substantial scientific reasons to doubt the scope of enablement, as set forth above. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. The specification does not describe any other polypeptides other than those whose amino acid sequences are shown in SEQ ID Nos: 1, 4, 5, 7 and 8, and since it is deemed to constitute undue experimentation to determine all the others, the disclosure is not commensurate with the scope of the claims and is enabling only to said polypeptides.

With respect to claim 48 which recites "a chimeric polypeptide .....wherein the SRC3-derived polypeptide inserted in a region of the host protein that is not essential to overall architecture of

folding..", the specification does not teach which regions of a host protein is essential to overall architecture of folding of the protein and which regions are not.

5b. Claims 53-56 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The written description in this case only discloses an isolated polypeptides with the amino acid sequence shown in SEQ ID Nos:1, 4, 5, 7 and 8, and a process for producing said polypeptides by conventional solid phase peptide synthesis. The specification does not disclose polynucleotides encoding the polypeptides of the instant invention, nor expression vectors comprising said polynucleotides, nor host cells comprising said expression vectors nor a method of producing the polypeptides of the instant invention by expressing a DNA encoding said polyeptides and recovering the polypeptide. Therefore the written description is not commensurate in scope with the claims drawn polynucleotides encoding the polypeptides of the instant invention, nor expression vectors comprising said polynucleotides, nor host cells comprising said expression vectors nor a method of producing the polypeptides of the instant invention by expressing a DNA encoding said polyeptides and recovering the polypeptide, as recited in claims 53-56.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117). The specification does not "clearly allow persons of

ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 115).

Support for the recombinant production of the polypeptide of the instant invention is provided in the specification on page 5, lines 25, through page 9, line 25, wherein general procedures for producing a protein recombinantly is disclosed. However, no disclosure, beyond mere recitations of general methods for recombinant production of proteins is made in the specification. The polynucleotide encoding the polypeptides of the instant invention have never been cloned, sequenced or put into an expression vector, thus it is impossible to produce the polypeptide of the instant Application recombinantly without first producing the encoding polynucleotide. Thus the mere mention of the recombinant production of the instant polypeptides is insufficient to support the generic claims as provided by the Interim Written Description Guidelines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645.

Therefore only isolated polypeptides comprising the amino acid sequence of SEQ ID NO:1, 4, 5, 7 and 8, produced by solid phase peptide synthesis procedures using automated peptide synthesizer meets the written description provision of 35 U.S.C. 112, first paragraph. As a result, it does not appear that the inventors expressed the polypeptides of the instant invention recombinantly or were in possession of a host cells transformed with polynucleotides encoding said polypeptides as recited in claims 53-56.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6a. Claims 37-57 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6b. Claims 37-43, 46, 48, 51-54 and 57 recite "an SRC3-derived polypeptide...", this is a relative term which renders the claims indefinite because, it is unclear how is this polypeptide derived from the third short consensus repeat (SCR3) region of the human complement receptor type 1 (CR1), should it consist 90% of the amino acids of this region, 50%, 5% or something else? Appropriate correction is required.

6c. Regarding claims 37, 43, 48, 52-54 and 57, the phrase "at least a portion of sequence... " renders the claims indefinite because it is unclear which portion of the 33 amino acids of the polypeptide shown in SEQ ID NO:1 is required and which portion is not . Appropriate correction is required.

6d. Claims 37, 43, 48, 52-54 and 57 recite "an SRC3-derived polypeptide having....." however, it is unclear if having is open or closed language. It is suggested that the claim be amended to recite "consisting" which is closed language or "comprising" which is open language

6e. Regarding claim 39 the phrase "...comprising a chemically reactive amino acid residue at least one of the carboxyl terminus and the amino acid terminus ..." renders the claim unclear and confusing, firstly, all amino acids are chemically reactive, and thus it is unclear what do the Applicants mean by this phrase, secondly, "at least one of the carboxyl terminus...", is also unclear, a polypeptide has only

one carboxyl terminus and amino terminus, so it is confusing what is meant by "at least one of the carboxyl terminus..... Appropriate correction is required.

6f. Claims 40 and 44 recite "...wherein the chemically reactive amino acid residues derivatized or derivatizable and ... a lysine derivative", however, it is unclear with what should the chemically reactive amino acid be derivatized. Which lysine derivative? Appropriate correction is required.

6g. Claims 42 is indefinite for reciting the phrase ".....wherein the polypeptide is altered at specific positions to remove chemically reactive amino acids", which specific positions to alter? How should these be altered? What is meant by chemically reactive amino acids?. Appropriate correction is required.

6h. Claims 49 recites "...wherein the host protein contains at least one SRC repeat", however, it is unclear which SRC repeat . Appropriate correction is required.

6i. Claim 48 recites "...wherein polypeptide is inserted in a region of the host protein that is not essential to overall architecture of folding ...", this renders the claim vague and indefinite, Applicants should recite the specific region of the host protein wherein the polypeptide of the invention is supposed to be inserted.

6j. Claims 37-43, 46, 48, 51-54 and 57 recite "an SCR3-derived...", the acronym SCR3 renders the claims vague and unclear. Reciting the full name of the region in the first independent claim would obviate this rejection.

Claim rejections-35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7a. Claims 37,39 and 51-57 are rejected under 35 U.S.C *§ 102*(b) as being anticipated by Fearon et al (U.S. WO 91/05047).

Fearon et al teach an isolated human complement receptor type 1 (CR1) protein and fragments thereof (see claims 41-52), polynucleotides encoding said CR1 protein and fragments, recombinant expression vectors comprising said polynucloetides and host cells transformed with the expression vector (see claims 1-29), a pharmaceutical composition comprising the CR1 protein, and methods of producing the CR1 protein recombinantly and by chemical synthesis, (see abstract, page 9 , lines 1-20).

Claims 37, 39 and 51-57 of the instant Application are drawn to a polypeptide derived from the third short consensus repeat (SCR3) region of the human complement receptor type 1 (CR1), polynucleotide encoding said polypeptide, an expression vector comprising said polynucleotide, a host cell comprising the expression vector, a pharmaceutical composition comprising said polypeptide, and methods of producing the polypeptide recombinantly and by chemical synthesis.

Therefore, Fearon et al reference clearly anticipates claims 37 and 51-57 of the instant Application. With respect to claim 39 which is directed to SCR3-derived polypeptide further comprising a chemically reactive amino acid residue at the carboxyl and amino termini, all amino acids are considered to be chemically reactive, therefore, the CR1 protein disclosed in Fearon et al reference anticipates this claim as well.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8a. Claims 48-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fearon et al (WO 91/05047) in view of Capon et al (U.S. Patent 5,116,964).

The teachings of Fearon et al have been set forth above, however, Fearon et al do not teach a chimeric polypeptide comprising a plasma protein and an SCR3-derived polypeptide.

Capon et al teach chimeric polypeptides comprising ligand binding partners fused to stable plasma proteins which is capable of extending the in vivo plasma half-life of the ligand binding partner, (see abstract and column 5, lines 14-20).

Therefore it would have been obvious to one of ordinary skill in the art at the time the instant invention was made to produce chimeric protein comprising a plasma protein and a polypeptide comprising a portion of the human complement receptor type 1 (CR1) because, Capon et al teach that chimeric polypeptides comprising a plasma protein and a polypeptide of interest are more stable and have extended in vivo half lives.

One of ordinary skill in the art would have been motivated at the time of the invention to produce chimeric protien comprising a plasma protein, and a polypeptide comprising a fragment of CR1 because, polypeptides corresponding to portions of CR1 possess

complement inhibitory activities and are active in the complement system to aid in the removal of foreign substances from host animals.

Conclusion

No claim is allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fozia Hamud whose telephone number is (703) 308-8896. The examiner can normally be reached on Monday-Friday from 8:00AM to 4:30PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Paula Hutzell, can be reached on (703) 308-4310.

Official papers filed by fax should be directed to (703) 308-4227. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Fozia Hamud
Patent Examiner
Art Unit1646
July 26, 1999

Prema Mertz
PREMA MERTZ
PRIMARY EXAMINER